

a<sup>1</sup>

peptide species that is poorly absorbed orally. Preferably,  $n$  is an integer from 3 to 6. More preferably,  $n$  is 5. More preferably still, the therapeutically active peptide species comprises Tyr-Gly-Gly-Phe-Met (SEQ ID NO: 1).

---

Please replace paragraph 14 with the following amended paragraph 14:

---

a<sup>2</sup>

**[0014]** In one embodiment, the present invention provides a pharmaceutical composition for use in the treatment of physiological conditions comprising a carrier moiety and a therapeutically active peptide species as defined above. The carrier comprises an aryl or alkyl group of sufficient length and/or steric bulk to inhibit rapid enzymatic degradation of the active drug species *in vivo*. A preferred carrier is selected from a group comprising cinnamoyl, benzoyl, phenylacetyl, 3,4-methylenedioxycinnamoyl, 3,4,5-trimethoxycinnamoyl, *t*-butoxycarbonyl, benzyloxycarbonyl, pivaloyl, N-9-fluorenylmethoxycarbonyl, and Fumaroyl. The carrier moiety is chemically linked to a therapeutic polypeptide of the general formula  $aa_n$ , where  $aa$  is an amino acid, or a chemical or structural variation thereof as defined above, where  $n$  is an integer from 2 to 40, and wherein the polypeptide is poorly absorbed orally. Preferably, in the drug composition of the invention,  $n$  is an integer from 3 to 6. More preferably,  $n$  is 5. In a particularly preferred embodiment, the polypeptide is Tyr-Gly-Gly-Phe-Met (SEQ ID NO: 1).<sup>1</sup>

---

Please replace paragraph 26 with the following amended paragraph 26:

---

a<sup>3</sup>

**[0026]** Met-Enkephalin (Tyr-Gly-Gly-Phe-Met) (SEQ ID NO: 1) is a naturally occurring pentapeptide ( $n = 5$ ) belonging to the endorphin class. It is known to be involved in the basic mechanisms of analgesia. It produces a transient analgesic effect when administered parenterally, but no effect has been observed when given orally. Its mechanism of action is believed to involve binding to opioid delta receptors in the brain. Met-Enkephalin is very rapidly degraded *in vivo* into a tetra-peptide that is subsequently metabolized. As for the pharmacokinetics of Met-Enkephalin, the plasma levels of the pro-drug, as well of those of the metabolites, are barely measurable, even when administered parenterally.

---